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PSORIASIS AND ARTHRITIS.

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As early as 1822 interest was focused on the association of arthritis and psoriasis, when Alibert first reported its occurrence. In 1888 Bourdillon produced the first detailed study in which the relation between the two was specifically examined. Since then numerous papers have been published, more particularly describing individual cases, in which the significance of the association has been debated. Until recent years, however, there has been no laboratory test which would distinguish between the two types of arthritis, uncomplicated rheumatoid arthritis and erosive arthritis with psoriasis, without taking the skin into account. Such a test was obviously necessary, since no clear cut clinical or radiographic picture of the erosive arthritis associated with psoriasis has been established. The advent of the Waaler-Rose Differential Agglutination Test (D.A.T.) for rheumatoid arthritis seems to have provided a solution, for this detects a specific abnormality in the serum of more than 80% of patients with rheumatoid arthritis (*Brit. med. J.*, 1956). It was the persistent absence of the Waaler-Rose phenomenon in the patients with psoriasis and arthritis seen before this study was started which first stimulated the writer's interest. The wide divergence of views shown in the literature about the association, and the scarcity of general surveys of the field, prompted a further review of the question in the light of this finding.

Material and Methods.

Forty-two patients with psoriasis and arthritis have been considered, comprising thirty-four with erosive arthritis, six with degenerative joint disease, one with rheumatic fever and one with gout. (The term " erosive arthritis " is used in preference to rheumatoid arthritis so that the issue may not be prejudged.)

The group has been contrasted with fifty-five unselected patients with rheumatoid arthritis and a positive D.A.T. An unselected group of 310 patients with psoriasis only has also been analysed from certain aspects for comparison. The patients with uncomplicated psoriasis were taken in sequence from a larger group and were drawn from skin clinics in the same area as that from which the arthritic patients came. In all cases the diagnosis of psoriasis was made by a dermatologist (Dr. D. S. Wilkinson) on those with uncomplicated psoriasis and confirmed by him on the arthritic patients. The purpose of this paper is to deal mainly with the dermatological manifestations : the arthritic features are only summarized since they are described in more detail elsewhere (Wright, 1956).

Incidence.

The incidence of erosive arthritis among patients with psoriasis is given as 8% (Tobias, 1939) ; 5·8% in males, 7·9% in females (Leczinsky, 1948) ; 7% (Ingram, 1954). In an urban population Kellgren *et al.* (1953) have estimated the incidence of rheumatoid arthritis as 3·1% (1·7% among men, 4·3% among women.) There seems to be general agreement therefore among dermatologists that the incidence of atrophic arthritis is higher in patients with psoriasis than in the general population.

TABLE I.—*Incidence of Psoriasis among Rheumatoid Patients.*

	%
Dawson and Tyson (1937)	2·6
Pringle (1938)	0·8
Bauer (1939)	3·0
Ragan and Tyson (1946)	8·0
Clemmesen and Arnsø (1952)	4·2
Gribble (1955)	4·2

Gahan (1952) estimated the incidence of psoriasis in the general population as at least 1% Bauer *et al.* (1941) using hospital patients as controls found psoriasis in 0·7% of non-arthritic controls. The figures for a higher incidence among rheumatoid patients in Table I only borders on statistical significance and no firm conclusion can be drawn from them. In the present series it was difficult to assess the incidence as the patients were drawn from several sources. However, thirty cases came from dermatological clinics in which about five hundred psoriatic patients have been treated in the course of six years. The estimated incidence of erosive arthritis among these psoriatic patients is therefore roughly 6%.

Sex Incidence.

Of the thirty-four patients with erosive arthritis, eighteen were men and sixteen women. This is of interest since both rheumatoid arthritis and psoriasis,

occurring singly, are commoner in women. The results in this group are shown in Table II.

TABLE II.—*Sex Incidence of Psoriasis, Rheumatoid Arthritis, and Psoriasis + Erosive Arthritis.*

Sex.	Psoriasis and erosive arthritis (34 patients) %	Rheumatoid arthritis (55 patients) %	Psoriasis (310 patients) %
Female	47·0	74·6	59·4
Male	53·0	25·4	40·6

Other series support the higher incidence among women of psoriasis and rheumatoid arthritis where it is occurring singly (Tables III and IV).

TABLE III.—*Sex Incidence of Psoriasis* (*Various Authors*).

Author.	Male (%).	Female (%).
Lane and Crawford (1937)	46·6	53·2
Madden (1939)	36·4	63·6
Ingram (1950)	41.0	59·0
Present series	40·6	59·4

TABLE IV.—*Sex Incidence of Rheumatoid Arthritis* (*Various Authors*).

Author.	Male (%).	Female (%).
Sclater (1943) :		
388 patients	30·5	69·3
Empire Rheumatism Council (1950):		
262 patients	38·2	61·8
Edinburgh Series (1950) :		
309 In-Patients	32·4	67·6
448 Out-Patients	22·3	77·7
Present Series :		
55 patients	25·4	74·6

Onset of Psoriasis.

Age.—In Fig. 1 the age of onset in patients with psoriasis and erosive arthritis is contrasted with those having uncomplicated psoriasis. At first sight there may appear to be a later onset in those with arthritis but this is not statistically significant.

Site.—There was no difference in the frequency of the sites of onset of the skin eruption in patients with erosive arthritis, the extensor surfaces of the limbs (usually elbows and knees) and the scalp being the commonest sites. The only unusual feature was the frequency of the nails as a target for initial lesions (16%). Two patients with erosive arthritis had no skin rash but marked changes of the nails beginning at the age of 58 years (a man) and 71 years (a woman) respectively. Only one patient in the uncomplicated psoriasis group had changes confined to the nails, a man whose lesions began at 70 years.

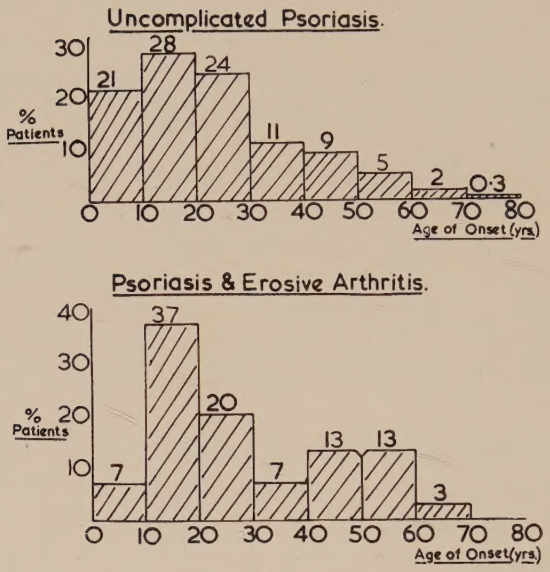

Uncomplicated Psoriasis.
% Patients
30
20
10
0
21
28
24
11
9
5
2
0·3
0 10 20 30 40 50 60 70 80
Age of Onset (yrs.)
Psoriasis & Erosive Arthritis.
% Patients
40
30
20
10
0
7
37
20
7
13
13
3
0 10 20 30 40 50 60 70 80
Age of Onset(yrs.)

Fig. 1.

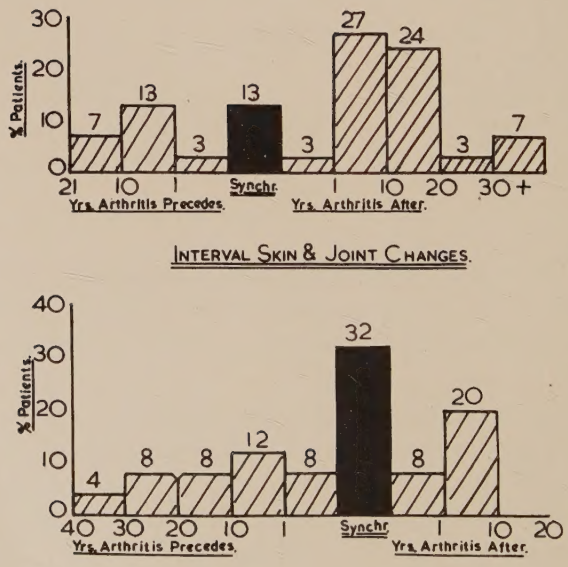

% Patients.
30
20
10
0
7
13
3
13
3
27
24
3
7
21 10 1
Synchr.
1 10 20 30+
Yrs. Arthritis Precedes.
Yrs. Arthritis After.
Interval Skin & Joint Changes.
% Patients.
40
30
20
10
0
4
8
8
12
8
32
8
20
40 30 20 10 1
Synchr.
1 10 20
Yrs. Arthritis Precedes.
Yrs. Arthritis After.
Interval Nail & Joint Changes.

Fig. 2.

Nail Changes.

In cases of psoriasis as a whole (including some with arthritis) the nails are said to be involved in between 10% and 25% of patients, the figure of 15% given by Pardo-Costello (1936) being about the average in the literature. Figures as high as 49·8% are however quoted (Crawford, 1937 and 1938). Among our group of patients with uncomplicated psoriasis 18% had changes of the finger nails (23% men, 14·7% women.) This contrasts sharply with the finding of nail changes in 87% of the patients with accompanying erosive arthritis.

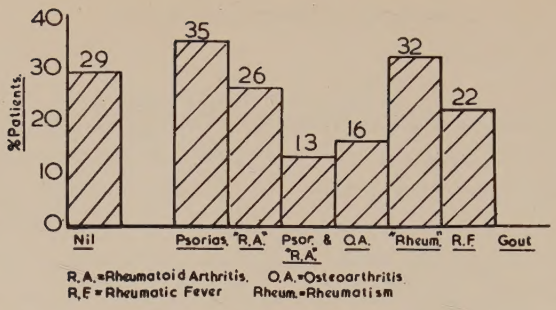
In some ways joint changes seemed to be more closely related to lesions of the nails than to psoriasis of the skin. Fig. 2 shows the onset of the arthritis related to changes in the skin and nails. Although skin changes and arthritis come on simultaneously in only 13%, nail changes were synchronous with arthritis in 32%. A closely related onset of the various manifestations (i.e. occurring within 12 months of each other) was seen in 19% between joint and skin changes, and 48% between joint and nail changes. Moreover, exacerbations were more often synchronous in nails and joints than in skin and joints.

In summary, in 53% nail and joint changes either developed simultaneously, or were subject to synchronous exacerbation. Only 24% had a similar relationship between the skin and joints ; an equal number claimed an inverse relationship, while in 52% no relationship was admitted. A topographical association between nail and joint changes was sometimes evident, but a similar association with the site of skin lesions could not be demonstrated.

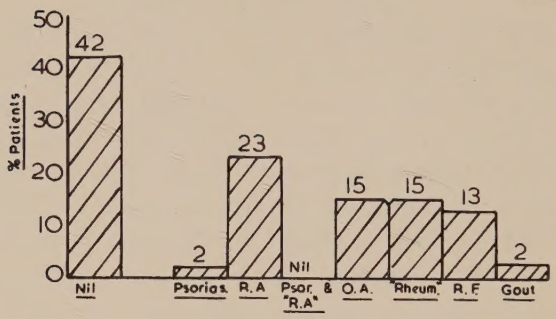
It will be noted from Fig. 2 that a quarter of the patients developed psoriasis after the onset of arthritis. It is tempting to suggest that some cases of erosive arthritis with a negative Differential Agglutination Test are destined to develop psoriasis. The only clue to this may be the family history, for 35% had a family history of psoriasis in the present series (Fig. 3).

Arthritis.

About equal proportions in each group had an acute onset (34%) and a pyrexial onset (22%). During the course of the disease the distribution of affected joints was the same in both groups with two exceptions. In the first place, among the psoriatic group, three patients had a clinical picture of ankylosing spondylitis with peripheral joint involvement. Secondly, there was a high incidence of distal interphalangeal joint involvement (58%). Relating the time of onset of the arthritis in these joints to that of changes in the skin and nails it can be seen that once again there is closer relationship with the nails than with the skin in the time of onset (Fig. 4). In no case however was the arthritis confined to the distal interphalangeal joints. When the distal joints were involved the fingers showed a broad spade-like appearance at the tips.

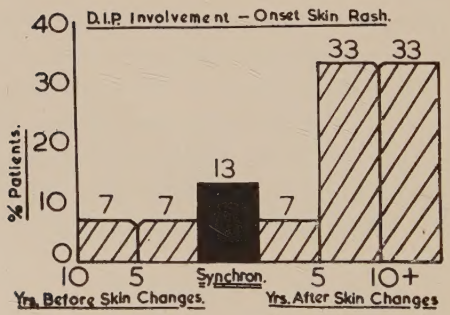


FAMILY HISTORY IN PSORIASIS & ARTHRITIS



FAMILY HISTORY IN RHEUMATOID ARTHRITIS

FIG. 3.



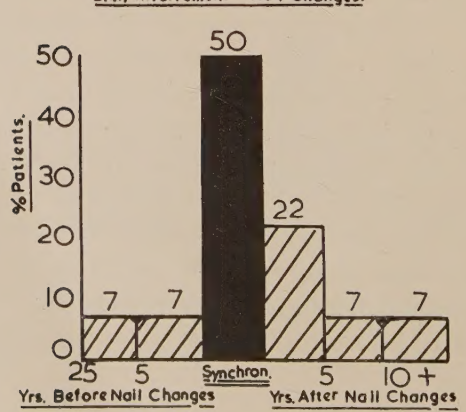


FIG. 4.

There is a less usual crippling form of the disease which was shown by three of these patients. The disease tended in fact to be either very mild or very disabling.

In only one patient with psoriasis and arthritis were subcutaneous nodules found, and he had a positive D.A.T. This is of interest since subcutaneous nodules are regarded by many as the most characteristic lesion of rheumatoid arthritis (Bauer, 1939 ; Bennett, 1943). Among the group with rheumatoid arthritis 17% had such nodules on examination, and 22% gave a history of their presence. Their complete absence among the patients with psoriasis and erosive arthritis with a negative D.A.T. strikingly differentiates them from patients with uncomplicated rheumatoid arthritis.

Skin Lesions.

There are varied reports in the literature on the course of the skin lesions in those patients in whom erosive arthritis is present. The majority however describe them as follows :

(i) Extensive—Barber (1931), Cole and Driver (1931), Van der Boijens (1939), Franks and Wallace (1942), Clarke (1950).
(ii) Often involving the palms or soles—Cannon (1934), Wassman (1949).
(iii) Often pustular—Kablak (1947), Ormsby and Montgomery (1954).
(iv) Resistant to treatment—Shlionsky and Blake (1936), Saunders (1942), MacKenna (1950).

Experience with this group did not conform to the above reported features.

(i) In only 34% had the psoriasis been extensive at any time. 41% had one or more spontaneous remissions. 11% had spontaneous partial remissions in which the psoriasis disappeared almost completely. 15% had almost complete remissions following treatment. In only 33% was there an absence of any lasting remission. These figures must however be regarded as only approximate since they depend on the subjective assessment of the patient. In 52% the psoriasis was minimal at the time of examination. In only three patients was it extensive ; two of these were completely bedridden owing to the arthritis and the third was severely disabled.

(ii) In only 19% were the palms or soles affected, and in one patient only were both affected. There was no relation in time or place between the affection of the skin of these parts and the arthritis except in one man who noticed his soles became affected for the first time 3–6 months before the onset of the arthritis.

(iii) The pustular form of psoriasis was not encountered in any patient with arthritis. (Cases of pustular bacterid were not regarded as psoriatic, but no evidence of arthritis existed in those that were seen by Dr. D. S. Wilkinson.)

(iv) The skin lesions were not resistant to treatment in the majority (71%).

However, it was noted that in those where such resistance was encountered the arthritis tended to be more severe. The patients with extensive psoriasis were treated with full dithranol and ultra-violet light regime. Many have recorded that the joints clear up with treatment of the psoriasis (Jeghers and Robinson, 1937 ; Epstein, 1939 ; O'Leary, 1943). Experience in the present series was sharply at variance with this finding. In fact only one patient had experienced this regression and it was probably significant that he had been at rest in hospital at the time.

Apart from involvement of the nails the frequency of sites affected does not differ substantially from published reports of unselected patients (Lane and Crawford, 1937 ; Madden, 1939).

Differential Agglutination Test (D.A.T.).

The D.A.T. in this series was done by a modification of the technique used by Rose *et al.* (1948) and Heller *et al.* (1955). It has been positive in not less than 80% of cases of rheumatoid arthritis and only in an extremely small percentage of non-rheumatoid arthropathies. Among the patients with psoriasis and erosive arthritis only two had a positive test—i.e. 94% were negative. One was the only patient in the series with nodules and tendon sheath effusions, and was also one of the four without nail changes.

Osteoarthritis, Gout, Rheumatic Fever.

The one patient with gout and the one with rheumatic fever who were examined showed no features that were not explicable as a mere coincidence of the psoriasis and joint condition. There were no unusual features of either disease.

The six patients with psoriasis and osteoarthritis were probably examples of a chance association also. The only unusual clinical feature was the involvement of the nails of all four men. There was no apparent relation between the onset and course of the lesions of the nails and skin and the arthritis.

Discussion.

Of the thirty-four patients with psoriasis and erosive arthritis 94% had a negative D.A.T. This suggests that the combination of psoriasis and erosive arthritis is more than the coincidence of two common diseases (as has long been suspected from the greater incidence of the combined diseases than would be expected) since the D.A.T. is positive in over 80% of patients with rheumatoid arthritis. It suggests that in those with a negative D.A.T. the arthritis either is modified by the psoriasis, or more probably is a distinct entity. The finding of tendon sheath effusions and subcutaneous nodules (both classical manifestations of rheumatoid arthritis) in only one patient of the series—one of the two with a positive D.A.T.—lends weight to the suggestion that these two were true rheumatoid patients, while the others formed a distinct group.

The major features of the erosive arthritis associated with psoriasis compared with uncomplicated rheumatoid arthritis were :

(i) It tended to be a milder disease than rheumatoid arthritis. A severe, crippling form did, however, occur.

(ii) The distribution of affected joints was the same except for a predilection for the distal interphalangeal joints which were more closely related to changes of the nails in time of onset than to lesions of the skin. A topographical association with nail changes was also seen sometimes.

(iii) There was a high incidence of sacro-iliac joint involvement.

The rarity in this series of the gross crippling form of psoriasis and arthritis compared with some other series may be due in part to the close association between our dermatological and rheumatological departments resulting in milder cases being included, and to the fact that large teaching centres from which most other reports have come would attract the grosser examples of the disease. Also, milder degrees of both were probably neglected by patients in the past and the series described here is obviously quite different material from that which seized the imagination of earlier writers.

From the dermatological point of view the interesting features of the arthritic group were :

(i) It was more often seen in men than in women.

(ii) The sites affected were the same at onset and in the course of the psoriasis whether joints were involved or not, except that the nails were affected in 16% of the arthritic group initially and in 87% at some time. This compared with 18% in those with psoriasis alone.

(iii) The arthritis at its onset and in its course was more closely related to the nail changes than to the skin lesions. A small proportion (13%) appeared to have a relation between the skin and joint manifestations as evidenced by synchronicity of onset or exacerbations.

(iv) The psoriasis was not usually extensive, although where this was so the arthritis was severe.

(v) The palms and soles were not usually affected.

(vi) In no case was pustular psoriasis present.

(vii) The psoriasis was not usually resistant to treatment except in those patients having severe arthritis.

(viii) In only one case was there an alleviation of joint symptoms when the skin was adequately treated, and this was probably fortuitous, since the patient was in hospital at the time .

Summary.

Three groups of patients have been analysed : 42 with psoriasis and arthritis, 55 with rheumatoid arthritis only (a positive D.A.T. was present), and 310 with psoriasis only. Of the first group eight with arthritis other than erosive arthritis

showed no feature which was not explicable on the chance coincidence of the two diseases, although the changes in the nails of the four men with osteo-arthritis was surprising. Of the thirty-four with erosive arthritis 94% had a negative D.A.T., and it is suggested that they form an entity distinct from rheumatoid arthritis. The dermatological and arthritic features of the syndrome "psoriasis with erosive arthritis" have been outlined in contrast with the group of patients with uncomplicated rheumatoid arthritis and uncomplicated psoriasis respectively. Possible reasons for the different clinical picture found in this group compared with other surveys are advanced.

I am indebted to Dr. D. S. Wilkinson, Dr. A. G. S. Hill and other consultants of Stoke Mandeville Hospital, where this study was carried out, for allowing me to study their patients. My thanks are due especially to Dr. D. S. Wilkinson and Dr. A. G. S. Hill for their invaluable help in the preparation and performance of this study in all its stages.

References.

Alibert, J. L. (1822) *Précis théorique et pratique sur les maladies de la peau.* 2nd édition. Paris : Caille et Ravier.
Barber, H. W. (1931) *Brit. J. Derm.*, **43**, 188.
Bauer, W. (1931) *New Engl. J. Med.*, **221**, 524.
——— Bennett, G. A. and Zeller, J. W. (1941) *Trans. Ass. Amer. Phys.*, **56**, 349.
Bennett, G. A. (1943) *Ann. intern. Med.*, **19**, 111.
Boijens, B. Van der (1939) *La Rheumatisme Psoriatique.* Paris : Thesis.
Bourdillon, C. (1888) *Psoriasis et Arthropathies.* Paris : Lecrosnier & Babé.
Brit. med. J. (1956) Leading Article, i, 1157.
Cannon, A. B. (1934) *Arch. Derm. Syph., Chicago*, **30**, 906.
Clarke, O. (1950) *Lancet, i*, 249.
Clemmesen, S. and Arnsø, E. (1952) In *Rheumatic Diseases.* Prepared by the Committee on Publications of the American Rheumatism Association. Philadelphia, London : W. B. Saunders Company.
Cole, H. N. and Driver, J. R. (1931) *Arch. Derm. Syph., Chicago*, **23**, 385.
Dawson, M. H. and Tyson, T. L. (1938) *Trans. Ass. Amer. Phys.*, **53**, 303.
Empire Rheumatism Council Investigation of Rheumatoid Arthritis. (1950) *Brit. med. J. i*, 799.
Epstein, E. (1939) *Arch. Derm. Syph., Chicago*, **40**, 547.
Franks, A. G., and Wallace, J. J. (1942) *Milit. Surg.*, **91**, 199.
Gahan, E. (1943) *Arch. Derm. Syph., Chicago*, **48**, 305.
Gribble, M. de G. (1955) *Ann. rheum. Dis.*, **14**, 198.
Heller, G., Kolodny, M. H., Lepow, I. H., Jacobson, A. S., Rivera, M. E. and Marks, G. H. (1955) *J. Immunol.*, **74**, 340.
Ingram, J. T. (1954) *Brit. med. J., ii*, 823.
Jeghers, H. and Robinson, L. J. (1937) *J. Amer. med. Ass.*, **108**, 949.
Kablak, K. (1947) *Ann. rheum. Dis.*, **6**, 230.
Kellgren, J. H., Lawrence, J. S., and Aitken-Swan, J. (1953) *Ann. rheum. Dis.*, **12**, 5.
Lane, C. G., and Crawford, G. M. (1937) *Arch. Derm. Syph., Chicago*, **35**, 1051.
Leczinsky, C. G. (1948) *Acta derm.-venereol., Stockh.*, **28**, 483.
Mackenna, R. M. B. (1950) *Brit. med. J., ii*, 207.
Madden, J. F. (1939) *Minn. Med.*, **22**, 381.
O'Leary, P. A. (1943) *Canad. med. Ass. J.*, **48**, 34.
Ormsby, O. S., and Montgomery, H. (1954) *Diseases of the Skin.* 8th edition, p. 304. London : Henry Kimpton.
Pardo-Costello, V. (1941) *Diseases of the Nails.* Springfield, Illinois : Charles C. Thomas.
Pringle, G. L. K. (1938) *Proc. R. Soc. Med. (Sect. phys. Med., and Sect. Derm.)*, **31**, 712.
Ragan, C. and Tyson, T. L. (1946). *Amer. J. Med., i*, 252.
Rose, H. M., Ragan, C., Pearce, E. and Lipman, M. O. (1948) *Proc. Soc. exp. Biol. Med., N.Y.*, **68**, 1.
Sclater, J. G. (1943) *Ann. rheum. Dis.*, **3**, 195.
Shlionsky, H. and Blake, F. G. (1936) *Ann. intern. Med.*, **10**, 537.
Tobias, N. (1939) *Int. Clin.*, **3**, 173.
Wassmann, K. (1949) *Ann. rheum. Dis.*, **8**, 70.
Wright, V., (1956) *Ann. rheum. Dis.* In press.

THE EFFECT OF HYDROCORTISONE ON STANDARDIZED SKIN-SURFACE TRAUMA.*

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If cellophane tape is applied to the skin surface and then sharply pulled off a fairly even spread of squames is found adhering to the gummed tape (Wolf, 1940). Pinkus (1952) showed that repeated stripping of a given area of skin resulted in progressive removal of keratin, layer by layer, until a glistening transparent surface was reached. He used this method in order to study, histologically, recovery from surface damage with particular reference to the burst of mitosis to be found in the deepest layers of the epidermis 48 to 72 hours after stripping. Lobitz (1954) recorded the changes in epidermal glycogen accumulation which followed this keratin stripping stimulus.

Presumably removal of nearly all the scales from the surface might increase the permeability of the epidermis, and therefore I thought that this particular damage and repair stimulus might lend itself to a study of the local action of hydrocortisone and possibly might be suitable as an assay method.

Method

A flat area of normal skin with uniform surface is chosen (usually the flexor aspect of the forearm) and half-inch wide cellophane tape is smoothed on to the skin for a length of about 8 cm. It is then peeled back from one end and sharply stripped off. A fresh piece of cellophane tape is applied to exactly the same area of skin and again it is immediately stripped off. This process is repeated until, after about 30 pulls, glistening macules appear on the skin surface which with further stripping become confluent. There is then an even pinkish-red surface which is glistening but not moist, and from which no further scales will come away. At this stage the stripping becomes sharply painful and any further attempts will result in excessive local damage with surface oedema and an axon-reflex flare at the edges of the strip.

Erythema persists in the strip for several days and it is neatly confined to the rectangle that has been denuded of scales. Towards 48 hours the redness begins to fade a little and thereafter the damaged surface becomes scaly and during the next week or two parakeratotic scales separate until normal compact keratin has been restored.

* Part of this paper was read at the 2nd Franco-British Reunion, July 1956.

Immediately after stripping the damaged area is divided into two or more parts ; one part is treated with the control of unmedicated vehicle, and the other parts with the hydrocortisone or other local applications. Applications are made 3 times in 24 hours if the experiment is prolonged. Dressings are applied to prevent friction of clothing, usually with a soft plastic material to cover the stripped area.

Results

In earlier trials results were rather variable, but with experience a technique has been developed which has given consistent results over the last 20 experiments in normal subjects.

About 4 hours from the first application of hydrocortisone at the start of the experiment some pallor is apparent at the edges of the strip while the control is uniformly red. By 6 hours the whole of the hydrocortisone-treated strip is paler than the control. At 12 hours from the start of the experiment the difference is maximal, the hydrocortisone-treated area often being as pale as normal skin (Fig. 1). By 24 hours this difference is becoming less as the control is fading, and the erythema starts to break through in the hydrocortisone-treated part of the strip. At 48 hours the difference between the treated area and the control is still present but less.

If at 24 hours from the start of the experiment applications are discontinued the previously treated area becomes red. The erythema breaks through after a few hours, and after about 6 hours from the last application the area may be as red as or redder than the control (Fig. 2). This gives a useful check that the original stimulus was equal throughout the strip. Various proprietary ointments and lotions containing hydrocortisone have been shown to suppress erythema in these experiments. No clear difference in activity between hydrocortisone acetate and the free alcohol has been shown, and in the effective range between 0·5 and 2·5% of hydrocortisone the results were about equal. With fluorohydrocortisone however it has been possible to show a greater effect. 0·1% fluorohydrocortisone ointment usually shows a more complete suppression of erythema of stripped skin than 1% hydrocortisone.

Glycyrrhetinic acid.—2% glycyrrhetinic acid in a greasy ointment base has been compared with its unmedicated ointment base, and with 1% hydrocortisone in the same base. In 5 experiments there was no difference between the ointment control and the area treated with glycyrrhetinic acid, whereas the hydrocortisone produced marked suppression of erythema.

Discussion together with Some Further Observations

The erythema.—The sustained redness of the stripped surface depends upon increase in transparency and upon dilatation of the sub-papillary vascular plexus. Both of these factors may be appreciated if the stripped surface is

viewed under the capillary microscope. The capillary loops of the papillae are seen end-on, and the network of the sub-papillary plexus is easily visible. The appearance is similar to that seen by Lewis (1927) after denudation of surface by blistering.

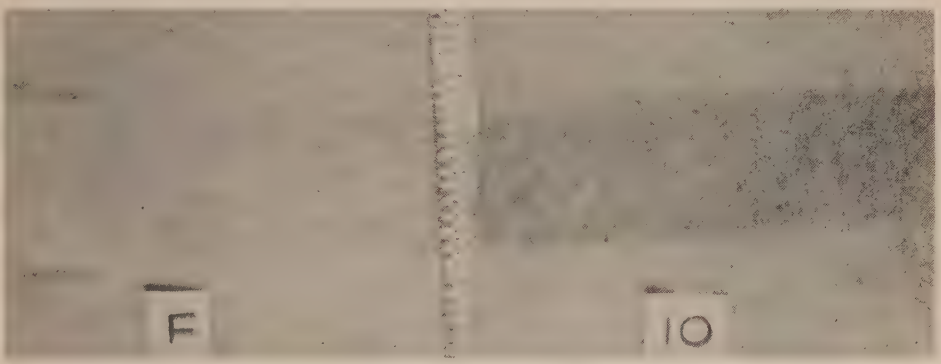

FIG. 1.—10 hours after keratin stripping. In half the strip ("F") 0·1% fluorohydrocortisone has inhibited vasodilatation, while in the control half ("10") treated with ointment base, there is erythema.

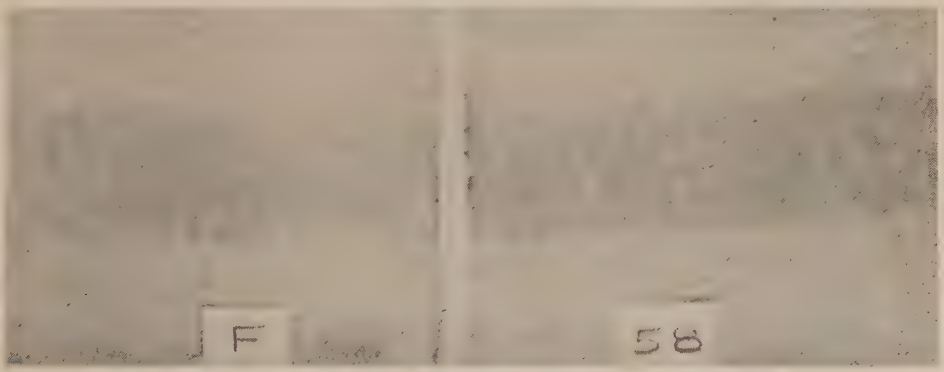

FIG. 2.—The same experiment as Fig. 1 at 58 hours, 10 hours after stopping all applications. Erythema has broken through in "F".

The erythema probably depends upon dilatation of the metarterioles and precapillary sphincters as occurs in chronic inflammation (Rothman, 1954) and not upon arteriolar dilatation such as occurs in acute inflammation.

The stripped surface remains dull pinkish red and perfectly flat; it is not appreciably hotter than the surrounding skin, and the erythema does not extend beyond the edges of the strip. The region is capable of showing a superimposed transient histamine-like response if the stripping damage is excessive or if a further stimulus is added. Thus, if, soon after stripping has

been completed, an irritating lotion is applied (some hydrocortisone lotions have irritating solvents in the vehicle), there is sharp pain followed within a few minutes by urticarial oedema of the stripped surface, and an axon-reflex flare spreading in blotches beyond the margins of the strip.

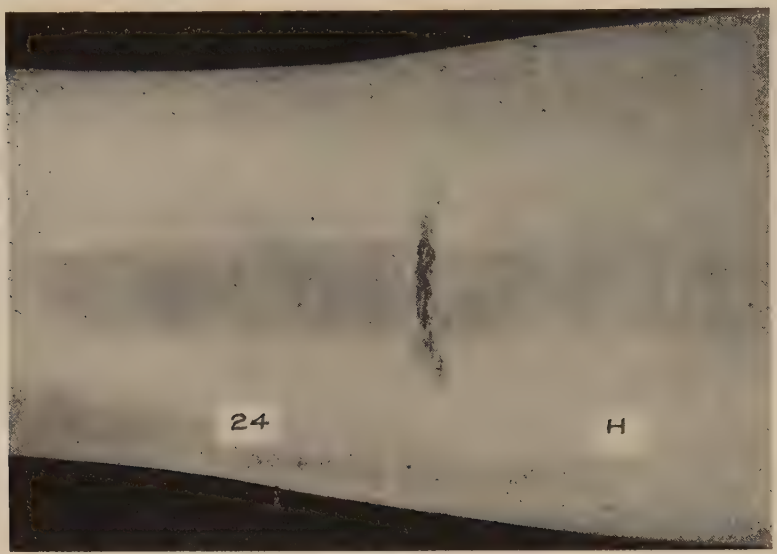

FIG. 3.—24 hours after keratin stripping the control (" 24 ") half of the strip is erythematous, while the other half (" H ") treated with 1% hydrocortisone is much less so.

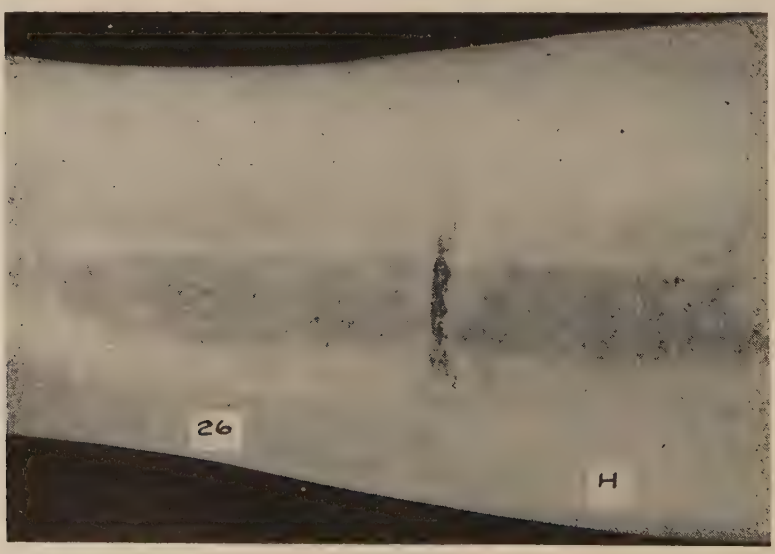

FIG. 4.—The same experiment as Fig. 3. After rubbing cedarwood oil onto the whole area, the control (" 26 ") is unaffected whereas " H " has become erythematous and shows arteriolar flare.

Under the capillary microscope a comparison can be made between hydrocortisone-treated and untreated parts of the stripped surface. When hydrocortisone is exerting its full effect, much less of the sub-papillary vascular plexus is visible in comparison with the control.

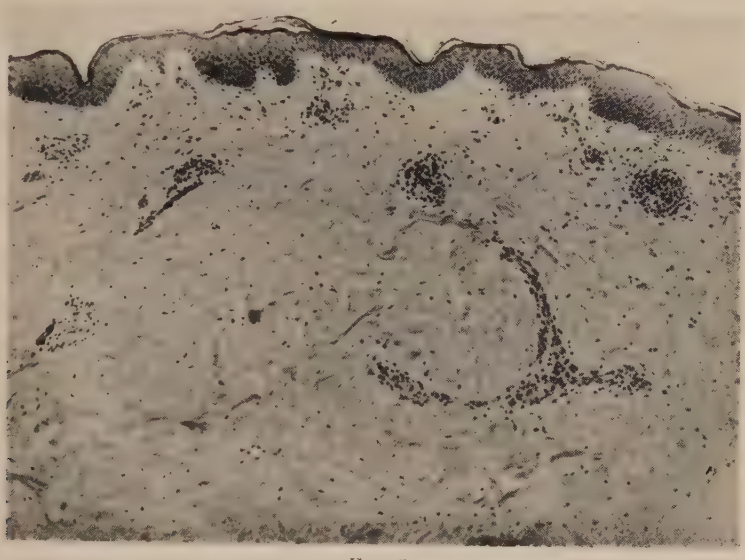

FIG. 5.

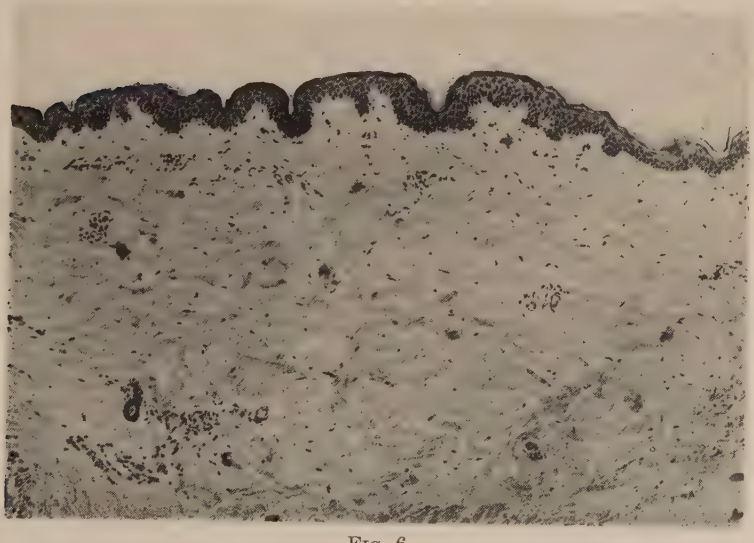

FIG. 6.

FIGS. 5 and 6.—Biopsies made from the same area of skin 48 hours after stripping. One half of the strip (Fig. 6) had been under treatment with 1·0% hydrocortisone ointment, while the other half (Fig. 5) had had the ointment base only. × 150.

In one experiment at 24 hours after stripping, hydrocortisone had inhibited vasodilatation in half the strip while the control, treated with ointment base, was dull red (Fig. 3). Cedar-wood oil was rubbed evenly over the whole strip, and, about 20 minutes later, a sharp burning pain together with redness and an axon-reflex flare spreading from the sides of the strip occurred only in the hydrocortisone-treated half of the strip (Fig. 4). This suggested that under the influence of hydrocortisone the stripped area had been held in a state of susceptibility to the effects of surface irritant greater than control.

Histological changes.—Paired biopsies were made under local anaesthesia ($\frac{1}{2}$% xylocaine) from different parts of the same stripped skin from the limbs of normal adult males, after control applications and after hydrocortisone application, at the following times from the start of the experiment : 24 hours —1 experiment ; 48 hours—5 experiments ; 60 hours—1 experiment.

A consistent difference between controls and hydrocortisone-treated parts of the strip was the heavier lymphocytic infiltrate around the capillaries of the upper part of the dermis in the controls (Figs. 5 and 6).

In two of the five cases where paired biopsies were made at 48 hours, the controls showed more numerous mitotic figures than the hydrocortisone-treated areas. In the other 3 cases this difference was not apparent. At about 60 hours much glycogen was present in the prickle cells of the middle layers of the epidermis in the control, whereas the hydrocortisone-treated area showed only minimal glycogen in the epidermis. The errors of sampling to be met with in making paired biopsies are, however, very great, and more observations are needed before it can be decided whether or not hydrocortisone slightly delays reconstitution of the epidermal surface.

General Discussion

Although surface applications of hydrocortisone have a suppressive effect on the inflammation in certain eczemas, experiments with various inflammatory stimuli applied to the skin have not given consistent results. If hydrocortisone is applied immediately after an erythema dose of ultraviolet light, the subsequent timing and intensity of the erythema shows no difference from controls (Everall and Fisher, 1952 ; Malkinson and Wells, 1954 ; Kanof, 1955) and these results contrast with the finding of some suppression of erythema after ultraviolet irradiation in patients under the influence of systemic steroid therapy (Järvinen, 1951 ; Holti, 1956). If applied after thermal burns (Kanof, 1955) hydrocortisone seems to increase the inflammatory damage. However, if the hydrocortisone is applied at least an hour before the inflammatory stimulus, the inflammation produced by ultraviolet radiation, mustard oil or nitric acid may be lessened (Scott and Kalz, 1956). With Grenz rays Kalz and Scott (1956) found that prior application of hydrocortisone could delay the onset of the late-appearing erythema.

In specifically sensitive patients Haxthausen (1956) used the electrophoretic patch to provoke allergic eczema in areas which were immediately afterwards treated with hydrocortisone. Partial suppression of the eczematous reaction was seen only in a minority of cases, but with $2\frac{1}{2}\%$ fluorohydrocortisone results were more definite.

All these experiments have involved the use of damage stimuli which evoke inflammation through complex and differing mechanisms. The stimulus provided by keratin stripping is capable of standardization, and the changes occurring in the skin over several days follow a predictable course. Another advantage of this method is that direct comparison can be made between one part and another of a uniform strip. The inflammation which follows stripping is related to the sequence of events leading up to repair of the damaged epithelial surface, but it has seemed advantageous to avoid the special inflammatory stimuli dependent upon allergy, radiation or chemical damage.

A characteristic feature of the action of hydrocortisone in these experiments is the delay of 4 to 6 hours following first application before suppression of vasodilatation can be seen. This delay corresponds fairly well with the time necessary for hydrocortisone labelled with radioactive carbon to reach the vascular region of the dermis as judged by radio-autographs (Scott and Kalz, 1956). The gradual return of erythema some hours after the last application of hydrocortisone is also characteristic, though the timing is influenced by various factors such as the removal of protective dressings and the cleaning of the surface.

There is some suggestion that during the earlier phases of the stripping experiments (the first 24 hours) when hydrocortisone is exerting its maximal suppression of inflammation, there may be some temporary delay in reconstitution of the surface. This difference is no longer apparent after about 48 hours, and histological differences between treated areas and controls were not definite enough to support any conclusions apart from the markedly less perivascular lymphocytic infiltrate in the hydrocortisone-treated area.

The vascular effect produced by hydrocortisone is probably not its only influence on inflammation (Allison *et al.*, 1955), yet this effect and its timing is highly characteristic of hydrocortisone, so much so that it is reasonable to use the keratin-stripping method as one means of determining whether a given application has or has not an action similar to that of hydrocortisone. The glycyrrhetinic acid ointments (Adamson and Tillman, 1955) tested by this method had none of the effect of hydrocortisone.

Summary

Most of the keratin can be removed from the skin surface by repeated stripping with cellophane tape. The denuded surface is transparent and there is persistent erythema.

Application of hydrocortisone after stripping is followed by inhibition of vasodilatation first apparent at about 4 hours and maximal at 12 hours. Erythema returns some hours after stopping hydrocortisone applications. Direct comparisons between one or more different applications can be made on the same strip. Ointments containing 2% glycyrrhetinic acid had none of the vascular effect of hydrocortisone.

Paired biopsies made from the same strip showed less perivascular small round cell accumulation in the hydrocortisone-treated areas than in the controls.

I am indebted to Dr. S. Gottfried, of Biorex Laboratories Ltd., for glycyrrhetinic acid ointments and their corresponding unmedicated bases.

I wish to thank Dr. A. C. Dornhorst for suggestions with the text.

I am grateful to Mr. R. J. Lunnon of the Institute of Dermatology for the photographs, and to Mrs. E. Woods for technical assistance.

References

Adamson, A. C. and Tillman, W. G. (1955) *Brit. med. J.*, ii, 1501.
Allison, Jr., F., Smith, M. R. and Wood, Jr., W. B. (1955) *J. exp. Med.*, **102**, 669.
Everall, J. and Fisher, L. (1952) *J. invest. Derm.*, **19**, 97.
Haxthausen, H. (1956) *Ibid.*, **26**, 111.
Holti, G. (1956) *Clin. Sci.*, **15**, 41.
Järvinen, K. A. J. (1951) *Brit. med. J.*, ii, 1377.
Kalz, F. and Scott, A. (1956) *J. invest. Derm.*, **26**, 165.
Kanof, N. B. (1955) *Ibid.*, **25**, 329.
Lewis, T. (1927) *The Blood Vessels of the Human Skin and Their Responses*. London : Shaw & Sons Ltd.
Lobitz, Jr., W. C. and Holyoke, J. B. (1954) *J. invest. Derm.*, **22**, 189.
Malkinson, F. D. and Wells, G. C. (1954) *Brit. J. Derm.*, **66**, 300.
Pinkus, H. (1952) *J. invest. Derm.*, **19**, 431.
Rothman, S. (1954) *Physiology and Biochemistry of the Skin*. Chicago : University of Chicago Press, p. 80.
Scott, A., and Kalz, F. (1956) *J. invest. Derm.*, **26**, 149.
——— ——— (1956) *Ibid.*, **26**, 361.
Wolf, J. (1940) *Z. mikr.-anat. Forsch.*, **47**, 351.

PYODERMIA CHANCRIFORMIS FACIEI.

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Pyodermia Chancriformis Faciei was first described by Hoffmann in 1934, although it appears to have been accepted as a clinical entity in France and Germany for some time before that. Krantz (1939) describing a case of his own and giving an excellent review of the subject, draws attention to the reports of other clinicians (Gougerot and Blum, 1929 ; Gaté and Treppoz, 1929 ; Gougerot *et al.*, 1930 ; Photinos, 1934 ; Stavropoulos, 1936 ; Richter, 1938 ; Gottron, 1937 ; Koch, 1939). Subsequently the condition has been reported on only a few occasions (Stryker, 1940 ; Griether, 1950 ; Laymon, 1954).

Hoffmann had first noted a case in 1914, in a young soldier who presented with a lesion on the temple which was button-shaped, superficially ulcerated with surrounding induration, and very suggestive of a syphilitic chancre. He was unable, however, to find any evidence of syphilis. In a second case, that of a 23-year-old female, a similar lesion was present on the right upper eyelid, recurring a year later on the left upper eyelid. *Staphylococcus aureus* in a pure culture was grown and again there was no sign of syphilitic infection. In his third case, in a man of 50, the lesion was thought to have followed an insect bite and resembled a squamous cell epithelioma. He referred briefly to further cases in which the characteristic ulcer had occurred on the nose, lower lip and buccal mucosa.

Dr. Bamber showed a case to the section of dermatology of the Royal Society of Medicine in 1935, under the diagnosis of extragenital chancre or a staphylococcal granuloma. The ulcer was again on an eyelid and on palpation it felt like a disc of cartilage ; *Staphylococcus aureus* was grown.

Three cases have been recognised at St. John's Hospital during the last two years and are reported here.

Case Reports.

Case 1.—A 33-year-old housewife presented on 4.iii.55 with an ulcerated lesion on the chin of 3 weeks' duration, which had started as a small yellow spot, suddenly increasing in size and ulcerating during the week prior to her first attendance, and reaching a diameter of about 2 cm. The lesion was indurated, the ulceration superficial with a raised rolled margin ; the base was covered with a crust which was easily removed to reveal a purulent discharge. Pain and discomfort were minimal and healing had taken place some 4 weeks later, leaving an irregular scar (which can be seen in Fig. 1). There was an associated regional adenitis, which soon settled. The total duration was about 7 weeks. She mentioned that she had had a similar smaller

Fig. 1

Fig. 2

ulcer on the left upper eyelid a year before this, and a soft white smooth scar was visible at this site.

The Wassermann reaction was negative at that time and again a year later.

Dark ground examination failed to reveal any spirochaetes. Bacteriological studies showed the presence of a coagulase positive staphylococcus, an anaerobic haemolytic streptococcus and gram negative bacilli but no diphtheria bacillus. The histology of a wedge of skin removed from the edge and including the base of the ulcer was that of a non-specific granuloma, showing ulceration with a dense infiltrate of lymphocytes and polymorphonuclear leucocytes with some eosinophils and histiocytes. Special staining failed to show bacteria.

She attended hospital again 3 months later with an ulcerated lesion of 3 weeks' duration on the inner aspect of the right upper eyelid, which she thought might have followed an insect bite. The ulcer was circular, about 1 cm. in diameter; the base was covered with a dark crust and there was some surrounding oedema (Fig. 1). Culture yielded a growth of *Staphylococcus aureus*. The lesion healed after a total duration of 8 weeks.

Local treatment did not appear to have any dramatic effect on the course of either lesion (Eusol: ½% aureomycin ointment; 1% hydrocortisone ointment). When seen one year later, the scar on the chin was unchanged and there was a faint smooth scar on the right upper eyelid with some permanent loss of eyelashes.

She was seen again on 18.vii.56, this time with a lesion affecting the inner aspect of the left lower eyelid of 2 days' duration. *Staphylococcus aureus* was again cultured and found to be sensitive to aureomycin, which was applied locally as a ½% ointment until healing had taken place. Although the classical chancriform lesion developed it was much reduced in size, was slower in development, and healed after a total duration of 4 weeks.

Case 2.—A 61-year-old female cook was first seen on 28.v.56 with a painless ulcer on the inner aspect of the right lower eyelid. This had been present for about 4 weeks and had started as a yellow spot which after a week or two had suddenly increased in size and ulcerated. There was a well defined rolled edge, the ulcer base was covered with a black crust and there was a slight serous discharge (Fig. 2). Induration was well marked and on palpation felt like the edge of a button imbedded in the skin. There was no glandular enlargement. The Wassermann reaction was negative. Healing was complete 16 days later, being very rapid in its early stages, so that the total duration was about 6 weeks. Local application of ½% aureomycin ointment was used. In addition there were present 5 non-tender slightly irritating firm brownish papules, averaging ½ cm. in diameter, and grouped together over the right pectoral region. One showed superficial ulceration. These all gradually subsided without treatment.

Case 3.—A 50-year-old male waiter was first seen on 1.vii.54 with a small spot of two weeks' duration just below the angle of the left mandible. This had enlarged to the diameter of 2 cm. a week later. The lesion was superficially eroded and the neighbouring submental gland enlarged. The Wassermann reaction was negative and repeatedly so on 5 occasions during the next 2 years. A heavy mixed growth of *Staphylococcus aureus* and micrococci was cultured: systemic penicillin had been given for 4 days prior to his first attendance and latterly ½% aureomycin ointment; healing was complete 3 weeks later, leaving a small soft white scar. Total duration was about 6 weeks.

The histology (Fig. 3) was that of an inflammatory reaction of the entire cutis consisting of lymphocytes, plasma cells, fibroblasts and mast cells. There was in addition a large number of eosinophils. A foreign body granuloma due to disintegration of a hair follicle was also seen. Special staining failed to show any bacteria, fungi or Leishman-Donovan bodies.

Fig. 3.

Clinical Features.

Pyodermia chancriformis faciei usually affects adults, of either sex, although Krantz (1939) quotes Covisa and Bejarano as having noted a similar type of lesion on the genitals of children. There was some doubt, however, as to whether they were describing the same entity. The lesion is usually solitary, although recurrences have been described as in my first case (Hoffmann ; Stryker). Most reported lesions have been on the face, and it therefore seems reasonable, although perhaps not strictly accurate, to retain the word faciei, which Hoffmann used in his original description. It apparently can occur elsewhere, Laymon having noted it on the shaft of the penis in association with exudative eczema of the genitals. By far the commonest site is the eyelid as in Case 1 and Case 2 and also in 8 of the 20 recorded cases in which the site of affection is mentioned (Hoffmann ; Stryker ; Greither ; Bamber ; Richter ; Gottron).

The initial lesion in both Cases 1 and 2 was a papulo-pustule, although it may be a vesicle. There may then be quiescence for a week or two after which ulceration occurs, with rapid enlargement and the development of characteristic features. This ulceration is usually superficial but it may be deeper when affecting the lip or genitalia (Hoffmann). The base is covered with a dark

crust, with a variable amount of exudate, more commonly serous than purulent. The edge of the ulcer is smooth and raised with minimal surrounding oedema and erythema, which may be more marked when the eyelid is affected. The whole lesion is freely movable over the subcutaneous tissue and on palpation feels like the hard edge of a button imbedded in the skin. Enlargement of the regional lymph glands is common, although variable in degree and may be absent. These enlarged glands are rarely tender. The lesion is also remarkably free from pain or discomfort.

It appears that when ulceration has taken place there is again little change for a week or two, but that once healing starts it is usually fairly rapid. The raised edge takes longer to flatten down, the small hard button of induration being palpable for some weeks after. The rapidity of healing was especially marked in Case 2. The total duration varies from 4 to 8 weeks. The resultant scarring is usually slight but can be more severe (Fig. 1).

Discussion.

Pyodermia chancriformis faciei appears to be a clinical entity with characteristic features in which the button-like ulcer closely simulates a syphilitic chancre, confirmatory evidence of syphilis being absent. Hoffmann commented on the significance of the occasional recurrence of the lesion as further evidence against a syphilitic aetiology and Gray (1935) in discussing Bamber's case mentioned that a primary extragenital chancre affecting the eyelid produces much more oedema and erythema. Although clinically there may be some resemblance to a squamous cell epithelioma, the subsequent course and histology rules this out. The possibility of the lesion resulting from accidental vaccination has not been borne out in the history of any of the reported cases and where investigations have been carried out with this possibility in mind, results have been negative (Krantz). Primary skin tuberculosis and cutaneous diphtheria have also been excluded bacteriologically and by the subsequent course of the lesion. Stryker reported negative results with serum agglutination tests for tularaemia and brucellosis.

The only regular finding is the isolation of *Staphylococcus aureus* in most cases. In the absence of any other positive findings there is therefore the likelihood that the lesion of pyodermia chancriformis faciei is the result of an abnormal tissue reaction to infection with this organism. In my first case and also in a case reported by Hoffmann there may have been some association with the bite of an insect. The progress of the lesion in the three cases described, with their pattern of quiescence, activity and subsequent rapid healing did not seem to bear any marked relationship to treatment directed against the infecting organism. It is possible that the most recent lesion in Case 1 was modified by treatment started within 2 days of its development.

Summary.

Three cases of pyodermia chancriformis faciei are described, and the literature reviewed. The condition appears to be a distinct clinical entity. The differential diagnosis is discussed. The part played by *Staphylococcus aureus* is still uncertain.

I should like to express my gratitude to Dr. R. H. Meara for supplying me with the details of Case 3, to Dr. H. Haber for his help with the histological interpretation, and to Dr. G. B. Mitchell-Heggs and Dr. I. Muende, for allowing me to report these patients who were under their care; also to Mr. R. J. Lunnon, photographer to the Institute of Dermatology, for the photographs.

References.

Bamber, G. (1935) *Brit. J. Derm.*, **47**, 244.
Gate, J. and Treppoz, R. L. (1930) *Bull. Soc. franç. Derm. Syph.*, **37**, 824.
Gottron, H. (1937) *Derm. Wschr.*, **105**, 1285.
Gougerot, H. and Blum, P. (1929) *Bull. Soc. franç. Derm. Syph.*, **36**, 70.
———, Burnier and Weile (1930) *Ann. Mal. vénér.*, **25**, 587.
Gray, A. M. H. (1935) *Brit. J. Derm.*, **47**, 245.
Greither, A. (1950) *Hautarzt*, **1**, 420.
Hoffmann, E. (1934) *Arch. Derm. Syph., Wien*, **170**, 403.
Koch, F. (1939) *Derm. Wschr.*, **108**, 191.
Krantz, W. (1939) *Ibid.*, **109**, 1203.
Laymon, C. W., Balogh, C. and Dixon, A. (1954) *Amer. J. Syph.*, **38**, 57.
Photinos, P. (1934) *Bull. Soc. franç. Derm. Syph.*, **41**, 1745.
Richter, R. (1938) *Dtsch. Arzt*, **1**, 337. (Quoted by Krantz, W.).
Sanchez Covisa, J. and Bejarano, J. (1934) *Actas dermo-sifilogr.*, **26**, 643.
Stavropoulos, M. J. (1936) *Bull. Soc. Pédiat. Paris*, **34**, 62.
Stryker, G. V. (1940) *Arch. Derm. Syph., Chicago*, **42**, 447.

URINARY INFECTIONS DUE TO 4,4′-DIAMINODIPHENYL SULPHONE THERAPY: REPORT OF THREE CASES

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One of the complications accompanying the protracted administration of antibiotics and chemotherapeutic agents is due to disturbance in the balance of the intestinal bacterial flora. The two most common are proliferation of *Candida albicans* and streptococcal enterocolitis. The former may cause nothing more serious than anal pruritus, the latter may prove fatal. One is amenable to mycocides, the other to appropriate antibiotics, determined by sensitivity tests.

Another toxic side-effect has recently come to our attention. It follows the prolonged administration of 4,4′-diaminodiphenyl sulphone (dapsone). Three patients receiving this medication developed urinary infections. When dapsone was discontinued and an appropriate antibiotic given each made a prompt recovery.

Diaminodiphenyl sulphone was synthesized by Fromm and Wittmann in 1908, but not until 1937 was it assayed for therapy in laboratory animals, with the result that it was found equal or superior to many sulphonamides and antibiotics for the treatment of tuberculosis, leprosy and various coccal infections. Empirically it has been successfully used in many toxic bullous eruptions, especially dermatitis herpetiformis and pemphigus. But why should its administration in therapeutic doses over long periods result in pyelonephritis rather than disturbances in bowel function such as are observed following the protracted use of antibiotics ?

Pharmacology.—A study of absorption and excretion was made. After the usual therapeutic dose dapsone is found in all tissues and body fluids, the liver and kidneys containing relatively high concentrations ; but individual variations in absorption and excretion occur in patients taking identical doses. It is probably completely absorbed, since 90% of the oral intake may be recovered from the urine and only a trace is detectable in faeces. Diasone, a chemically related sulphone, is about 50% absorbed, 48% being recovered in the urine and 44% in the faeces. Sulphetrone is poorly absorbed, only 10% being found in the urine and 80% in the faeces. Promacetin is likewise poorly absorbed, the larger fraction being found in the faeces. All sulphones are cumulative and regular rest periods during therapy are advisable. The activity of all is dependent on their breakdown in the gastro-intestinal tract to dapsone, and high con-

centrates of the latter have been found in the blood and urine of patients treated with these derivatives.

Toxicity.—Hypochromic anaemia is the most common indication of toxicity to the sulphones. Haemolytic anaemia has been reported in guinea-pigs given promin (Higgins, 1943), and in rabbits following sulphetrone (Brownlee, 1948.) Anaemia is not a feature following prolonged administration of dapsone. This is perhaps because it is excreted almost exclusively in the urine ; whereas its derivatives, being present in large measure in the bowel, inhibit proliferation of those bacteria essential for the autosynthesis of B complex vitamins, and thus indirectly interfere with haematopoiesis.

Other toxic reactions are rare. At the U.S. Public Health Service Hospital at Carville, Louisiana, more than 1100 patients have taken one or another dapsone derivative for long periods without a single case of serious illness or fatality attributable to them. In Nigeria, Barnes and Barnes (1951) have reported 7 cases of jaundice and 1 death in 153 patients treated with dapsone, all associated with exfoliative dermatitis. Agranulocytosis and similar haemal dyscrasias have not been observed.

Minor disturbances such as repeated attacks of erythema nodosum, arthralgia, and peripheral neuritis due to intolerance of sulphone therapy are common. Side reactions involving the urinary tract, which is the specific purpose of this report, are not common. On the other hand one must take into account amyloid nephrosis, long recognized as a leading cause of death in leprosy. It has been our experience that over prolonged periods patients with slight albuminuria require lower than ordinary doses of dapsone.

Case Reports.

Case 1.—A man 45 years of age had dermatitis herpetiformis, successfully treated for five years with sulphapyridine in doses of 2 to 3 g. daily. However in August 1954, because of leukopenia attributed to the medication, he was started on dapsone in daily doses of 150 mg. This controlled the disease as well as had the sulphapyridine, so that after four months this was reduced to 100 mg., and after another month to 50 mg. daily.

In February 1955 pyuria and haematuria developed. Cultures made from the bladder and ureters showed haemolytic staphylococci, coagulase negative, which were sensitive to erythromycin and tetracyclin. The infection responded promptly to oral medication with furadantin. Treatment with dapsone was not discontinued.

In March the patient experienced a recurrence of the cystitis. Cultures again showed haemolytic staphylococci, sensitive to erythromycin. However the administration of erythromycin was ineffective, and in addition furadantin, to which there had been prompt response a month previously, was likewise without benefit. Chloromycetin, given orally, resulted in rapid recovery.

The dapsone was now stopped and sulphapyridine resumed for eight weeks. At this time dapsone was again substituted, and within two days the patient developed urinary frequency and again cultures showed haemolytic staphylococci. This attack also responded promptly to chloromycetin.

The patient has been on sulphapyridine since with complete control of his dermatosis and urinary complaints.

Case 2.—A man aged 66 years had pemphigus vulgaris of several years' duration which had failed to respond satisfactorily to steroid hormones. In August 1954 he was started on dapsone in doses of 150 mg. daily. There was prompt improvement and in three months the dose was reduced to 100 mg. and subsequently to 50 mg. This controlled the eruption. In late January he complained of burning on micturition, and the urine showed 150–200 pus cells per high power field with clumping. There were no erythrocytes. The dose of dapsone was reduced to 25 mg. daily, and within two weeks bullae reappeared on the scalp. The dose was then increased to 50 mg. without improvement. The urine now showed 10-15 leucocytes per high power field. Again the dapsone dosage was gradually reduced, and in July discontinued. In August the urine was normal.

Case 3.—A man aged 75 years had leprosy. In November 1954 he was started on dapsone, 100 mg. daily and gradual clinical improvement followed. In August 1955 medication was discontinued because of strangury and frequency of micturition. A culture from the bladder showed haemolytic streptococci, sensitive to aureomycin. Cystoscopy showed severe cystitis which responded promptly to aureomycin.

On November 15 1955 dapsone was resumed in doses of 100 mg. every second day. Within a month symptoms of cystitis recurred, associated with prostatitis. Discontinuation of dapsone and administration of aureomycin was again followed by prompt recovery.

Conclusions.

The cases reported indicate that 4,4′diaminodiphenyl sulphone when administered by mouth is capable of provoking urinary infection by organisms resistant to it.

References.

Barnes, J. and Barnes, E. J. (1951) *Leprosy Rev.*, **22**, 54.
Brownlee, G. (1948) *Lancet, ii* 131.
Fromm, E. and Wittmann, J. (1908) *Ber. dtsch. chem. Ges.*, **41**, 2264.
Higgins, G. M. (1943) *Amer. J. med. Sci.*, **205**, 834.

OBITUARY

ACHILLE CIVATTE.

With the death of Civatte, dermatology has lost one of its most distinguished figures, and one who was greatly loved as a man of great modesty activated by the highest principles.

Civatte was born at Sisteron, Haute-Provence, in 1877 and was the seventh generation of doctors in his family. He became the pupil of Brocq and under his guidance wrote his thesis on parapsoriasis in 1906. Then followed a long period abroad in which he studied in London, Berlin, Hamburg, Breslau and Vienna, during which he acquired his interest in histopathology. On his return to Paris he came to complete his studies under Darier to whom he became assistant at the Collége de France and the Hôpital Saint-Louis and within a short time his disciple, co-worker, confidant and life-long friend.

Civatte's scientific work was considerable. Apart from innumerable interesting and rare cases which he reported at the Société française de Dermatologie, one may mention particularly his original researches on parapsoriasis, lichen scrophulosorum, lupus erythematosus, the fibroma *en pastille* and the facial poikiloderma which bear his name; but it is in cutaneous histopathology that Civatte particularly distinguished himself. He made remarkable contributions regarding the primordial vesicle of eczema, on the subjects of psoriasis, prurigo, tuberculides, lichen planus, carcinoma, and most recently on acantholysis and its value in the diagnosis of pemphigus and other bullous dermatoses. When he died, Darier entrusted to Civatte the task of revising his *Précis de Dermatologie* and the fourth edition appeared in 1947. Very soon afterwards were published the first parts of Civatte's *Atlas d'Histo-Pathologie Cutanée*, a masterly work to which he devoted his remaining energy. Since 1922, Civatte was the curator of the celebrated histological museum at the Hôpital Saint-Louis which he himself inaugurated and of which he was always the animating spirit.

Civatte enjoyed world-wide authority. He was a member of nineteen dermatological societies, among them the British Association of Dermatology. In France he was president of the Société française de Dermatologie in 1938 and a member of the Académie Nationale de Medecine since 1934. In 1931 he was presented with a medal, the occasion of a moving ceremony at the Hôpital Saint-Louis at which were gathered his many friends as a mark of their great esteem and affection.

Although his influence on French dermatology was great, establishing the essential importance of histopathology, Civatte had few direct pupils, for his manner was reserved and his work not readily accessible to a great number; but his few pupils were carefully chosen and include Dupont of Louvain, Vilanova of Barcelona and Percival of Edinburgh. For those who overcame his reserve he was revealed as a noble, sincere and loyal friend. His somewhat austere aspect concealed a great sensitivity and in the way of his countrymen, an ardent spirit. He had a deep feeling for good writing, painting and particularly classical music and as Dupont has said, he was "*un grand bourgeois traditionaliste qui jugeait de toutes choses avec un sain réalisme*".

We express to Madame Civatte and their three children our most sincere sympathy and to all French dermatologists the sorrow with which we see this great man depart from our midst.

BOOK REVIEWS.

Essentials of Dermatology*

Since the 4th edition published in 1952, Tobias's *Essentials* has expanded by another 55 pages. It can no longer be carried at a stretch in the jacket pocket. The author has an undoubted talent for expressing facts concisely yet readably but will have to be more drastic with his pruning if the book is to retain its present useful status of portable guide and friend to the busy practitioner.

The author's approach is to sick people with skin diseases rather than to individual skin lesions. The concept of multiple factors in aetiology is well expressed and a reasonably balanced share of the blame is allotted to material and psychological factors. For example, with pompholyx the functional variety is number one on his list, and mycotic, contact and toxic forms are placed second, third and fourth respectively. With lichen simplex he does not stop at hydrocortisone, tar and x-rays, but recommends that emotional conflicts should be discussed and possible solutions found.

The foot of each page is not littered with references. Instead, there are selected references on special subjects at the foot of a few pages and a useful 4-page reference library for dermatologists near the index. At the end of each chapter there is a section dealing with the nursing aspects of the conditions mentioned.

Grammar and spelling are unusual in some places. " Data " and " criteria " are used as if singular, and we read of sweat retension, fulgerated, lichen sclerosis, sellate naevus, and port wine *agi*omas.

There are a few new half-page illustrations in colour from the Abbott Laboratories. There seems no very clear reason why these particular conditions have been selected for polychromatic display. A picture of neurofibromatosis in monochrome on page 590 is more informative than the coloured illustration some 560 pages away, in plate 2. The monochrome illustrations are mostly of excellent quality but a panel of dermatologists might not correctly diagnose figures 4, 7, 163 or 206. A peculiar false modesty on page 38 is not present on page 151.

Many European dermatologists would dispute that in erythema nodosum the tubercle bacillus only plays the role of a secondary invader due to lowered resistance (page 43). There is some confusion over the terms " sarcoid " and " sarcoidosis ". On page 320 under the heading " Sarcoid Reaction " it is stated that sarcoids are not related to sarcoidosis, but on page 321 under the heading " Sarcoidosis " the two terms are used synonymously.

The only side effect of importance with chloroquine is said to be inability to accommodate (page 61) : visual halos and blanching of the hair are not mentioned. There is also no mention of cortisone therapy for lichenoid gold eruptions (page 116). Film-going dermatologists may be surprised to see scabies given the synonym "Seven Years' Itch " (page 207).

It is surprising to find a 4% benzocaine preparation recommended for acute solar dermatitis (page 283). It may be difficult for patients with pruritus ani to follow the advice on page 258 to " relax more, worry less, and avoid anything that upsets the peace of mind ". It does not seem right to treat strawberry haemangiomata for the reason that " most parents regard these lesions as stigmata " (page 576) : cannot the dermatologist modify this parental attitude by advice and a favourable prognosis ?

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* *Essentials of Dermatology* (5th Edition). Norman Tobias. Philadelphia : J. B. Lippincott. Pp. 651, 211. illus. 11 in colour. Price 64*s*. net.

Selecting these few items for friendly criticism in no way detracts from the overall acceptance of this book as a sound practical guide to the essentials of dermatology. It is beyond serious criticism in its general format and content. The production of five editions in fifteen years is an indication of its popularity. B. F. R.

A Volume for Teachers—and Others.*

The name of this book is wisely chosen, for this is not just another text or reference book of the usual type. It has been written with the desire to link such pre-clinical and clinical teaching as the student or practitioner may have received with the specialized knowledge of the dermatologist. It is the type of work which our predecessors would have named " On Dermatology ", and the preposition would have been of considerable significance.

In their preface the authors comment on our common experience, that students are interested in and can readily understand, for example, diseases of the kidney, because they have been taught much about that organ before they see their first case of nephritis ; but, in most medical schools, there has been no similar " build up " before the pupils come to the Skin Department where they are at once launched into a study of pathological processes involving a very complex organ with only the most rudimentary knowledge of its physiology. Pillsbury and his colleagues therefore devote the first ten chapters of their book to a somewhat didactic study of the anatomy and physiology of the skin ; their style is more reminiscent of the lecture theatre than the library—some facts being stressed, others being omitted—the whole integrated to the ultimate purpose of getting the student to understand the viewpoint of the clinical dermatologist. At the end of each of their chapters there is a series of paragraphs in heavy print summarizing what has gone before. The theme then changes to a consideration of fundamental matters in mycology, bacteriology, anaphylaxis and allergy. All this pre-clinical information is contained in 174 pages.

Then, the authors introduce the topics of clinical examination and regional diagnosis, types of skin lesions and the distribution patterns of eruptions. It was at this point that your reviewer began to feel disturbed. " For whom," he asked himself " is this book written ?" If for students, they cannot understand much of the section on regional diagnosis full as it is of brief references to maladies beyond their knowledge ; if for qualified men with some knowledge of dermatology, the balance is wrong—e.g. 19 pages on maladies of the lips and oral cavity compared with a very inadequate reference to alopecia and only about 8 pages concerning eruptions on the trunk. In a subsequent edition the authors would be well advised to reconsider the material in this section and its position in the book. In contrast, the succeeding chapter concerning types of skin lesions is beautifully presented.

The section on treatment is as vulnerable to the attacks of the prejudiced as any similar compilation, but regarded dispassionately it is a good synopsis of old and new knowledge. In the remaining 900 pages most skin diseases are effectively studied, sometimes in the text-book manner but more often discursively. The arrangement of subjects is unusual : attention is first given to infections (bacterial, spirochaetal, fungal, viral and rickettsial), the papulo-squamous rashes and the usual congeries of lichens, purpura, pemphigoid eruptions, and the rest. It is not until Chapter 49 that hereditary maladies are described, this topic being followed by chapters on " Psycho-cutaneous Medicine ", reactions to physical agents and—surprisingly—a final chapter on industrial dermatitis. Many will consider that these last chapters could more effectively be placed elsewhere in the book.

Of the important features one may select the excellent black and white illustrations,

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* *Dermatology*. D. M. Pillsbury, W. B. Shelley and A. M. Kligman (1956) Philadelphia and London : W. B. Saunders Company. Pp. 1331. Illus. 564. Price 140*s*.

the amusing diagrams (a particular feature of the Pennsylvania School), the views on infantile dermatitis in atopic subjects which may come as a shock to those of us who once studied Fundamentals of Medical Dermatology, the acceptance of the mast-cell hypothesis in regard to the aetiology of urticaria, the chapters on metabolic diseases, lupus erythematosus and diseases of the nails ; each reader will have his own preferences and many will prefer other chapters and other subjects. On the other hand, any critic is at liberty to carp at what he doesn't like and no authors can write a volume 1331 pages in length without being absolutely certain that (except in regard to the index, which is excellent) they are laying themselves wide open to attack. But the real point is—what is the value of this book to English-speaking dermatologists outside the U.S.A. ? Your reviewer would not tell any student to buy it unless the latter was convinced that he was going to be a dermatologist ; but there are several chapters, particularly in the early part of the book, to which the attention of students could profitably be drawn. For selective reading the book is valuable for registrars and senior registrars. Nevertheless the important aspect of the work, and the one which will justify its existence, lies in its value to teachers ; to these it is warmly commended. For example, if preparing a lecture on a topic which is not one's pet subject, perusal of this book will save a good deal of wide reading to verify the facts one requires : if undertaking the more difficult task of preparing a talk on a complicated matter concerning which one knows a great deal, the book will help one to discern the wood from the trees. Further, in preparing a course of lectures, much help can be obtained from consideration of the scheme the authors have adopted, the matters they have stressed and those they have omitted.

From these and from other points of view this book is a worthy successor to the two impact-making books (*Modern Clinical Syphilology* and *Fundamentals of Medical Dermatology*) for which Pillsbury's predecessor J. H. Stokes was primarily responsible; if without impertinence one may say so, the traditions of L. A. Duhring are being well maintained.

R. M. B. MacK.

The Year Book*

The authorship of the Yearbook has undergone a change : Dr. Sulzberger has left, and Dr. Victor Witten has joined R. L. Baer as junior author. Naturally, the general form of the book, and happily its high standard, remain much the same as ever, though the familiar reader may fancy he can detect change in literary style.

This year the authors' first chapter is on x-ray and Grenz-ray therapy. Although it is understandable that this chapter cannot aim at completeness there are some disappointing omissions. For example, for the x-ray treatment of acne vulgaris the authors say that cases must be carefully selected—but proceed to mention only that other treatment should have failed and that the patients should have reached the age of 17 ; all other methods of selection are left to the imagination. In the radiotherapy of epitheliomas also the authors give very little guidance in the selection of cases and do not mention the importance of bone or cartilage involvement. If, as they say in another part, it is not their purpose to review details, it at least seems a pity that they have stopped short of points such as those mentioned above, since the selection of cases is described in some detail in other paragraphs. Grenz rays gain considerably more favourable mention than would be acceded by most British dermatologists. This may well be because we have not sufficiently tried this type of treatment and the comments of these authors, writing from their own experience, suggest that the new apparatus requires a further assessment in this country.

F. R. B.

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* *The Year Book of Dermatology and Syphilology* (1955–56). Edited by Rudolf L. Baer and Victor H. Witten. (1956) London : Interscience Publishers Ltd. Pp. 480. Fig. 61. Price 49*s*.

Ulcus Cruris*

The interest of dermatologists in ulceration of the leg is comparatively recent and we search in vain for any reference to the subject in the textbooks of Bateman, Plumbe, Rayer, Cazenave and Schedel, Erasmus Wilson and Radcliffe-Crocker. Perhaps because the profession during the last century was obsessed with the importance of varicose veins in the aetiology of the condition it was thought proper to leave its treatment to such few surgeons as were interested in it. There are however some notable exceptions to this policy for both Hunt (1859) and Kaposi (1880) made valuable contributions to the subject. During the last few decades the interest of dermatologists in leg ulcers has quickened and they have become more aware of their responsibility in the treatment of this common and disabling condition. Prosser White was one of the first to appreciate that leg ulcers are often a sequel of deep venous thrombosis and he was the first to advocate the use of massage in their treatment.

The publication of Professor Piulachs's monograph is therefore of importance to many dermatologists. Chief Professor of Surgery in the Faculty of Medicine in Barcelona, one of the centres of vascular surgery, he has taken a special interest in ulceration of the leg and writes with authority. The book suffers a little in its translation from Spanish which has no doubt delayed publication considerably. Certainly it is somewhat unfortunate that no references are later than 1953 and most are prior to 1949, for the subject has advanced a little during recent years especially from Cockett's anatomical investigations and the tracer studies of Helen Payling Wright. However, it is an important book which gives us the author's views, some highly original, founded on a wide experience of the subject and which opens up the European literature, often difficult of access to English readers.

Venous, arterial and neurotrophic ulcers are considered. The author believes that with venous ulcers an insufficiency of the deep veins is almost always present and that 90% of such ulcers are post-thrombotic. He considers at length the problem of arteriovenous shunts in the aetiology of varicose veins, a subject on which he has done much original work. As might be expected, there is little new in the sections on treatment but it is dealt with fully. For venous ulcers lumbar ganglionectomy is believed to be contraindicated and extirpation of the ulcer and immediate grafting is recommended. Various methods of treating varicose veins are described including the injection of sclerosing fluids and the stripping operation and in certain patients ligation of the popliteal or the superficial femoral vein is advocated. Many will not agree with these views. It is, moreover, surprising to find the local application of penicillin, sulphonamide and streptomycin recommended.

This is a well published book containing a large number of photographs, many of which are informative and of high quality. An excellent monograph on a difficult subject, it should be read by all those interested in peripheral vascular disease.

S. T. A.

References.

Hunt, T. (1859) *A Guide to the Treatment of Diseases of the Skin : with Suggestions for their Prevention.* 4th Ed. London : Richards.

Kaposi, M. (1880) Hebra's *On Diseases of the Skin.* Vol. V. London: The New Sydenham Society.

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* *Ulcers of the Legs.* By P. Piulachs. (1956). Springfield, Illinois. : Charles C. Thomas. Oxford : Blackwell Scientific Publications. Pp. 574. 303 Illus. Price £5 17*s.* 6*d.*

CORRESPONDENCE

The Editor, 'The British Journal of Dermatology.'

Sir.—Although one can agree with much that Dr. Hellier says (p. 342), his letter should not go unanswered.

There is a body of opinion, and I believe a growing one, that medical education must be more concerned with the training of minds and habits of thought than with the inculcation of "facts". A purely technical medical training has long been impracticable although it is still attempted in some medical schools; but the recent report from the Royal College of Physicians and articles which have appeared in the medical press show abundantly that these ideas are being rapidly given up. The dermatological post-graduate student should be a M.R.C.P. and will in the ordinary course of events be at least 25 years of age. I suggest that if by this time he still needs mainly lectures and set courses he has been badly chosen for consultant work; and contrariwise, that the good trainee will by this age have developed his own methods of study and will not benefit from overmuch organisation.

The registrars of St. John's Hospital for Diseases of the Skin, to which the Institute of Dermatology is affiliated, normally do out-patient sessions for only a proportion of their time, the numbers of patients being limited to permit adequate study of the cases. The branches of their study are not laid down by rules or set courses, since it is considered that, with advice and some guidance, they can be safely left to develop their interests and, within broad limits, to decide for themselves how much time they should devote to various aspects of their subject. Within the Institute are departments of general pathology and bacteriology, histopathology, mycology, radiotherapy and biochemistry, all entirely devoted to, and adapted to, the study of dermatological problems. Through part-time teachers it is not difficult to bring post-graduate students into liaison with those in fields allied to dermatology in the schools which are linked with the University of London. Surely it is better to make these opportunities available to the man who has the initiative to reach out for them, than to attempt to cover the whole corpus of dermatological knowledge by courses of organised instruction?

I should welcome a committee of the kind Dr. Hellier suggests, for we can all learn something from it; but I suspect that the solution is to train more men at the better equipped and larger centres rather than at those universities where the undergraduate student must claim the chief attention. In the peripheral centres he can "make the tea" and sit at the feet of a great dermatologist and a proportion of his time spent in this way will be by no means wasted.

Yours etc.,
F. Ray Bettley.

London,
November, 1956.

CURRENT LITERATURE

VITAMIN B_{12} IN THE TREATMENT OF PSORIASIS. Muscardin, L. (1956) *Cronache dell'Idi*, **5–6**, 115.

Vitamin B_{12} has been credited with various beneficial effects apart from its haemopoietic activity. Within a few years of its isolation it brought about the usual successes in other fields that are expected of all new drugs. Its " lipotropic " action has recently been directed against xanthelasma palpebrarum, the newest disease to fall victim to its magic. (Do medicines with a number always have a greater effect than those with only a name ?)

Thirty-one patients with psoriasis have been treated with this vitamin and the results assessed. They are equivocal : 7 excellent results, 12 good. 1000 μg. a day for 10–12 days were given to most of the patients. The best results were observed in patients who complained of itching. The reviewer distrusts the itching psoriatic as a subject for drug trials. But at least the treatment is harmless. D. S. W.

DUHRING'S DISEASE IN INFANCY. Zar, E. (1956) *Arch. ital. Derm. Sif.*, **27**, 353.

Two straightforward cases of dermatitis herpetiformis in infancy treated successfully with cortisone. D. S. W.

THE PROBLEM OF OTITIS EXTERNA. C. Keogh and B. Russell. (1956) *Brit. med. J.*, i, 1068.

A joint otological and dermatological investigation demonstrated that otitis externa is usually caused by pathogenic cocci or by intestinal organisms, the reservoirs of infection being the nasal vestibules, staphylococcal folliculitis, paronychia, areas of infected dermatitis, and the anogenital region. Prevention depends on avoiding digital transference of organisms from these foci of of infection ; a high standard of personal hygiene is essential.

Treatment consists of eliminating the infective state, treating any associated skin disorder, removing irritating detritus, and relieving any persistent aural pruritas with local and systemic remedies. B. A. T.

THE CLINICAL VAGARIES OF THE HERPES VIRUS. R. T. Brain. (1956) *Brit. med. J.*, i, 1061.

In this Watson-Smith Lecture, a complete and authoritative account is given of the herpes virus in all its aspects, including trigeminal neuralgia associated with herpes simplex, primary herpetic gingivo-stomatitis, primary herpetic infections in infants and the primary infections of genitals and eyes. The relationship of the virus to encephalitis and similarity of disseminated herpes to generalised vaccinia are also discussed. The varying degree of infectivity of the virus, from epidemics of Kaposi's varicelliform eruption to the endemic herpes simplex is a puzzling vagary of the herpes virus. B. A. T.

FLEA INFESTATION AS A CAUSE OF PAPULAR URTICARIA. R. M. Bolam and E. T. Burtt. (1956) *Brit. med. J.*, i, 1130.

The parasitic theory of causation of papular urticaria, suggested by Jonathan Hutchinson in 1879, has gained increased support in recent years. The writers consider that almost all cases can be explained by parasitic infestation although often obscure at first sight. Thirty cases were investigated at hospital and at the homes of patients. In 21 cases fleas were found or were hatched out from dust samples and included five different species. Attention to disinfestation resulted in a clearance of the eruption and kept 14 of the 21 patients free. B. A. T.

SUSPENDER DERMATITIS AND NICKEL SENSITIVITY. C. D. Calnan and G. C. Wells. (1956) *Brit. med. J.*, i, 1265.

Contact dermatitis from allergy to nickel has long been recognized, but its frequency among women has not been reflected in recent literature nor has the high incidence of patches of dermatitis from metal suspender clips been adequately stressed. It is estimated that 3% of women attending skin departments show this allergy. Four hundred cases are here analysed and the primary sites of nickel dermatitis listed. Patterns of the secondary eruptions are worked out and are of vital importance from the points of view of both diagnosis and treatment. The introduction of plastic or nylon suspenders is advocated. B. A. T.

OBSERVATIONS ON ACNE, SEBORRHOEA, AND OBESITY. S. Bourne and A. Jacobs. (1956) *Brit. med. J.*, i, 1268.

The incidence, sites and severity of acne in 2720 soldiers are described and correlated with colouring, the degree of obesity and dandruff. The incidence and severity of acne are the same in men with all grades of dandruff and the value of shampoos in the management of acne is doubtful. Colour of hair is unrelated to the incidence of acne. Most acne occurs at 18–19 years, the face being most commonly affected. During adolescence, acne is not related to obesity but men over the age of 20 with acne tend to be heavier than those without it. B. A. T.

SOAP AND THE SKIN. I. Martin-Scott and A. G. Ramsay. (1956) *Brit. med. J.*, i, 1525.

The properties of a neutral soap have been investigated in the laboratory and in hospital. After skin had been washed with this soap, the skin fat factor showed no change from the normal and the pH of the skin remained unaltered. It thus had no denaturing effect on the skin whose protective acid mantle remained intact. The neutral soap was found to be innocuous to persons intolerant of ordinary toilet soaps. About 100 sufferers from eczema were able to enjoy using this neutral soap with impunity. B. A. T.

NYLON STOCKING DERMATITIS. C. D. Calnan. (1956) *Brit. med. J.*, i, 147.

Dermatitis from nylon stockings is rare. It is the dye and not pure nylon that produces sensitization. In stocking dermatitis, the sites commonly affected are the dorsa of the feet, the backs of the knees and the inner parts of the upper thighs.

Six characteristic cases are described, the dermatitis being traced to an azo dye.

B. A. T.

TREATMENT OF CONTACT DERMATITIS DUE TO HANDLING ANTIBIOTICS. R. M. Morris-Owen. (1956) *Brit. med. J.*, i, 654.

Antibiotic dermatitis is an occupational hazard of doctors and nurses. Classical " desensitization " has hitherto been used as the method of treatment.

Patients receiving minute doses in the first phase of desensitization were much less vulnerable to contact and this transient tolerance to contact can be maintained by frequent repetition of the same small dose. Five case histories are presented in which minute tolerated subcutaneous doses of penicillin or streptomycin are able temporarily to suppress specific allergic reaction to skin contact. Maintained daily treatment with such doses may continuously suppress reaction despite the subject's regular handling of either antibiotic. This " cover " régime may ultimately induce a relatively lasting tolerance. B. A. T.

THRUSH NAPKIN RASHES. J. P. Bound, (1956) *Brit. med. J.*, i, 782.

Attention is drawn to the frequency of thrush infections as a cause of napkin rashes. Oral thrush was present in less than one-third of 47 cases. The mothers of infected babies had a significantly increased incidence of vaginal thrush. B. A. T.

LUPUS ERYTHEMATOSUS: CLINICAL AND HAEMATOLOGICAL STUDIES IN 77 CASES. R. H. Marten and E. K. Blackburn. (1956) *A.M.A. Arch. Derm. Syph., Chicago.*, **73**, 1.

This excellent summary gives a standard by which one can measure one's own findings in this disease ; though the abstractor continues to admire the number of cases, even of the discoid type, in which the authors can find L.E. cells. J. K.

CUTANEOUS APPEARANCE OF PORPHYRIA BY ULTRAVIOLET LIGHT. Theodore Cornbleet. (1956) *A.M.A. Arch. Derm. Syph., Chicago*, **73**, 34.

The author has noted in 3 cases examined under Wood's light, patches of a deep purplish hue on areas usually exposed to light. This may be seen on areas of apparently normal skin as well as in hyperpigmented parts. The abstractor, in a case recently seen, was not able to confirm these findings. J. K.

CUTANEOUS MANIFESTATIONS OF MULTIPLE MYELOMA. Samuel M. Bluefarb. (1955) *A.M.A. Arch. Derm. Syph., Chicago*, **72**, 506.

This is an excellent summary of the cutaneous lesions associated with multiple myeloma with details of those seen in 4 cases. These lesions can be divided into a specific (extra-medullary

plasmocytomas and tumours of the skin due to extension from bone lesions) and non-specific (cutaneous manifestations due to abnormal proteins, cytopenias, toxic eruptions and those due to involvement of internal organs, e.g. kidneys, lungs and nervous structures). There is an extensive bibliography. J. K.

PROGRESSIVE SYSTEMIC SCLEROSIS: VISCERAL MANIFESTATIONS IN GENERALIZED SCLERODERMA. W. N. Piper and E. B. Helwig. (1955) *A.M.A. Arch. Derm. Syph., Chicago*, **72**, 535.

Generalized scleroderma is not strictly a dermatosis but may affect connective tissue wherever it exists. The skin manifestations usually induce the patient to consult a dermatologist in the first place, though involvement of viscera may precede the appearance of skin changes. The symptoms and clinical findings are not diagnostic but depend on the site affected and the degree of involvement. A review of the records and 27 necropsies of patients with circumscribed scleroderma showed no evidence of systemic involvement. J. K.

SENILE KERATOSES AND INTRAEPIDERMAL EPITHELIOMAS. L. van der Meiren and G. Achten. (1955) *Arch. belg. Derm. Syph.*, **11**, 95.

The authors have studied 112 biopsies of senile keratoses and classified them according to Hinselmann's findings in precancerous lesions of the cervix uteri. Their results show that 42% showed simple abnormality of the epidermis (thickening without cellular changes), 27% showed aggravated abnormality (thickening with loss of regularity of arrangement of cells and with cell nests but little or no alteration in the cells themselves) and epithelioma *in situ* (having in addition numerous cells, abnormal in size or in their nuclei but with intact basal layer). In 4 of these cases histological evidence of commencing squamous epithelioma was found. J. K.

EFFECT OF CHLOROQUIN TREATMENT ON THE CORTICOSTEROID CONTENT OF BLOOD AND URINE IN A CASE OF ACUTE SYSTEMIC LUPUS ERYTHEMATOSUS. S. Lapiere and H. van Cauwenberge. (1956) *Arch. belg. Derm., Syph.*, **12**, 1.

The patient improved under treatment and during this period the 17-hydroxycorticosteroid content of the blood and urine increased while the 17-ketosteroids in the urine diminished. While further observations are necessary it would seem that chloroquin can stimulate the production of ACTH. J. K.

LABORATORY STUDIES IN SYSTEMIC LUPUS ERYTHEMATOSUS. Stanley L. Lee. (1956) *A.M.A. Arch. Derm. Syph., Chigago*, **73**, 313.

Systemic lupus erythematosus may rightfully be considered a disease of protein metabolism. In the laboratory four anomalous activities may be detected in the gamma globulin fraction of blood plasma. They are: false positive serological tests for syphilis, positive direct antiglobulin tests, the presence of an anticoagulant factor, and the L.E. cell factor. Each of the first three is present in roughly one fourth to one third of patients and more than one may be present in the same patient. The L.E. cell factor is the commonest finding. Recent work seems to show that the development of systemic lupus erythematosus may be predicted in patients with chronic false positive serum tests for syphilis. J. K.

DISCOID LUPUS ERYTHEMATOSUS TREATED WITH PLAQUENIL. Theodore Cornbleet. (1956) *A.M.A. Arch. Derm. Syph., Chicago*, **73**, 572.

PLAQUENIL IN THE TREATMENT OF DISCOID LUPUS ERYTHEMATOSUS. Henry M. Lewis and Gerald M. Frumess. (1956) *A.M.A. Arch. Derm. Syph. Chicago.*, **73**, 576.

Plaquenil is the trade name for 7-chloro-4-[4-(N-ethyl-N-β-hydroxyethylamino)-1-methyl-butylamino] quinoline, a drug similar to chloroquin. In all 29 patients were treated and the results so far indicate that plaquenil is at least as effective as mepacrine or chloroquin and is less toxic. J. K.

URTICARIA PIGMENTOSA AS A PROBLEM IN DIAGNOSIS. REPORT OF TWO CASES, ONE WITH SYSTEMIC INVOLVEMENT. P. Brodeur and L. I. Gardner (1956). *New Engl. J. Med.*, **254**, 1165.

Urticaria pigmentosa in two infants is described. In one of them both liver and spleen were enlarged and mast cells were found in the bone marrow and peripheral blood. The amount of histamine and heparin was much greater than normal.

It is suggested that urticaria pigmentosa is due to a congenital error, perhaps enzymic, in the metabolism of histamine or heparin and that mast cell proliferation is secondary to this.

A. D. P.

STEROID THERAPY OF HYPERCALCAEMIA AND RENAL INSUFFICIENCY IN SARCOIDOSIS. R. W. Phillips and D. P. Fitzpatrick. (1956) *New Engl. J. Med.*, **254**, 1216.

The problem of hypercalcaemia in sarcoidosis is reviewed, attention being given to the danger of renal damage occurring. The authors report two further cases treated successfully with cortisone and advise that it should be used early to avoid the risk of renal insufficiency developing.

A. D. P.

HYPERLIPEMIC XANTHOMATOSIS WITH ASSOCIATED OSSEOUS GRANULOMA. H. J. Koch and J. S. Lewis. (1956) *New Engl. J. Med.*, **255**, 387.

A case of xanthomatosis in a woman aged 60 is described in detail. Some features were characteristic of essential xanthomatosis of the hypercholesteraemic type, others of the Schüller-Christian syndrome and yet others of hyperlipaemia.

The authors consider that when " the clinical and laboratory findings of the case are summarized a new syndrome emerges that has characteristics common to all three of the primary xanthomatoses ".

A. D. P.

SCLERODERMA (PROGRESSIVE SYSTEMIC SCLEROSIS), ASSOCIATED WITH CANCER OF THE LUNG. S. M. Jonsson and J. M. Houser. (1956) *New Engl. J. Med.*, **255**, 413.

The interesting feature in this report is the development of an adenocarcinoma of the lung in a woman aged 31, many years after the onset of scleroderma. The lesion appeared two months after treatment with cortisone was begun.

A. D. P.

POLYNEURITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS. C. Scheinberg. (1956) *New Engl. J. Med.*, **255**, 416.

Full details are reported of a patient with systemic lupus erythematosus. The nervous system was involved and there was widespread polyneuritis, confirmed histologically. The author believes that the polyneuritis was caused by pressure on nerve fibres by an amorphous material, similar to haematoxylin bodies.

A. D P.

ICHTHYOSIFORM ATROPHY OF THE SKIN IN HODGKIN'S DISEASE. F. Ronchese and D. C. Gates. (1956) *New Engl. J. Med.*. **255**, 287.

A further case of ichthyosiform atrophy of the skin in a man with Hodgkin's disease is reported. A remarkable feature was that the skin became normal or almost normal on five occasions after treatment with blood transfusions, x-ray and nitrogen mustard.

A. D. P.

SYNDROMES ASSOCIATED WITH " ALLERGIC " VASCULITIS. R. G. McCombs, J. F. Patterson and H. E. MacMahon. (1956) *New Engl. J. Med.*, **255**, 251.

The literature of vasculitis is briefly reviewed and details of 30 patients with " allergic " vasculitis are given. In more than half there was a history of allergy.

Allergens included drugs, infective agents and tumours, and evidence of vasculitis was provided by skin biopsy. One or more of the following was present in each case—haematuria, albuminuria, purpura, erythema nodosum, dermatitis, dermatomyositis, urticaria, eosinophilia, arthralgia, oedema, pyrexia, loss of weight, pleurisy, paraesthesiae, gastro-intestinal bleeding and increase in the serum globulin with decrease in the serum albumen in some.

The response to steroid therapy was excellent.

A. D. P.

TREATMENT OF PEMPHIGUS WITH ACTH, CORTISONE AND PREDNISONE. L. Reznick, W. F. Lever, G. C. N. Frazier. (1956) *New Engl. J. Med.*, **225**, 305.

Between 1950 and 1954 twenty-five patients with pemphigus were treated with ACTH, cortisone or prednisone and the results are here reviewed.

Of the patients with pemphigus vulgaris ten are now living and the authors state that " no patient need die of pemphigus ". That death may result from steroid therapy is, of course, admitted, and this is thought to have caused the death of one patient and possibly two others.

The importance of early treatment and adequate dosage in pemphigus vulgaris is emphasized. Thirty to forty units of ACTH daily as an 8-hour infusion to start treatment is advised and the

dose should be increased if necessary. Side reactions were frequent, including mental changes in 11, bacterial infection in 7 with septicaemia in 2 and vertebral fractures in 4. Of minor manifestations it is said " a maximum clinical response was usually not achieved until they appeared ".

A. D. P.

DEMONSTRATION OF TISSUE AUTO-ANTIBODIES IN THE BLOOD SERUM OF PATIENTS WITH CERTAIN SKIN DISEASES. V. Wagner, G. Šeba and B. Hrušková. (1956) *Dermatologica*, **112**, 25.

In three patients with lupus erythematosus, in two with pemphigus vulgaris, one with acrodermatitis chronica atrophicans and one with impetigo herpetiformis (Hebra), the authors have searched for auto-antibodies in serum with the help of collodion agglutination with various human tissue antigens. They have succeeded in demonstrating auto-antibodies whose occurrence and titres were for the greatest part in correlation with clinical damage of organs. The hypothesis of an auto-immunization in the pathogenesis of L.E. and other skin diseases is discussed. (Authors' summary.)

J. F. S.

THE SIGNIFICANCE OF ORGANIC ACIDS FOR THE NEUTRALIZATION OF ALKALI. J. J. Zoon, A. Hovenkamp and L. H. Jansen. (1956) *Dermatologica*, **112**, 21.

The amino-acids take a subordinate part in the alkali neutralization of the skin. This neutralization in so far as it is not caused by carbon dioxide and these amino-acids, is for the greater part due to organic acids. It appears that at least 70–90% of these organic acids are lactic acid. (Authors' summary.)

J. F. S.

THE TREATMENT OF THE EPITHELIOMATA OF CHRONIC ENDEMIC ARSENICALISM WITH DEMECOLCINE. E. E. Tello and L. V. Ferraris. (1956) *Dermatologica*, **112**, 230.

In the province of Córdoba, Argentina, many wells contain enough arsenic to cause much chronic arsenical poisoning, and among other manifestations keratoses, going on to epithelioma, are common. This gave the authors an exceptional opportunity of testing the new alkaloid from colchicum, acetylmethylcolchicine, or démécolcine. They used it in the form of a 0·1% ointment in six patients, who presented in all 30 assorted cancerous and precancerous lesions, and of these 29 were completely cured, and only one, a squamous-celled epithelioma, was refractory.

J. F. S.

MYCOSIS FUNGOIDES IN THE LIGHT OF ITS CLINICAL COURSE. F. Miedziński and I. Golebiowska. (1956) *Dermatologica*, **112**, 119.

On the basis of a comparative analysis of two of the authors' own observations (one mycosis fungoides (*tumeurs d'emblée*) and one m.f. (erythrodermica), and with reference to the literature, they discuss the question of whether the former should be regarded as a neoplastic process. They emphasize that the clinical symptoms alone are not sufficient to distinguish it from a reticulosarcoma, but that the histological picture, for the time being the only definite criterion, shows it to be a reticuloendotheliosis. On the basis of extensive investigations, it is still to be proved how far a m.f. can become a reticulo-sarcoma. M.f. seems to have a strongly retarded progress in older persons, perhaps owing to the weaker reactivity of the reticuloendothelial system in old age. (Authors' summary.)

J. F. S.

A CASE OF ELASTOMA INTRAPAPILLARE PERFORANS VERRUCIFORME PRESENTING THE PICTURE OF MORBUS KYRLE. G. Miescher. (1956) *Dermatologica*, **112**, 307.

He describes a case corresponding clinically to the classical picture of Kyrle's disease, but histologically showing the same process as in a case that was recently published as elastoma intrapapillare perforans verruciforme, i.e. a primary formation of an intrapapillary mass made up of elastic fibres, with bionecrosis of the thus altered papillae or groups of papillae and their elimination through the epidermis, which reacts to it with acanthosis, hyperkeratosis and parakeratosis. An identification of these histological findings with those given by Kyrle and other authors of hyperkeratosis follicularis at parafollicularis in cutem penetrans is as yet not possible, and needs further investigation. The question therefore remains open of whether the present case is only a variant of elastoma intrapapillare perforans verruciforme which has been classified as Morbus Kyrle, or whether Morbus Kyrle itself is actually identical with the former.

J. F. S.